A Novel, Concentrated, High loading Nanoparticle-based Formulation of Progesterone for Emergency Traumatic Brain Injury, Princeton Docket # 12-2766

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Technology description

Unmet Need

Progesterone is a water-insoluble steroidal hormone that is a promising therapeutic for treating traumatic brain injury (TBI). However, it is difficult to formulate the steroid for emergency administration due to its hydrophobicity, crystallinity, and poor bioavailability. In the literature, many different nanoparticulate formulations for progesterone have been described, but the highest concentration and drug loading reported remain low at 12 wt% of the particle solids, reaching 2.6 mg/mL progesterone in the aqueous dispersions (Yuan et al. Colloids Surf. B. Biointerfaces 60(2), 174-179 (2007)). A high concentration of progesterone is needed in the formulation, such that a relatively large dose can be administered in a small volume. Furthermore, quick delivery of the steroid to the bloodstream is desired, since administration of progesterone within 24 hours of the TBI produces the most benefit (Roof et al. Exp. Neurol. 138, 246-251 (1996)). It is known that progesterone rapidly crosses the blood-brain barrier and reaches equilibrium with plasma (Xiao et al. Crit. Care 12(2), R61 (2008)), thus quick release of the steroid to the bloodstream from a vehicle is favorable.

Proposed Solution and Potential Commercial Markets

Researchers in the Department of Chemical and Biological Engineering, Princeton University have successfully used Flash Nanoprecipitation (FNP) to produce polymeric nanoparticles (NPs) at a base concentration of 10 mg/mL of the steroid. The progesterone-loaded nanoparticles were made using only components that are classified by the FDA as GRAS (generally recognized as safe). The resulting nanoparticles are 300 nm in diameter with 24 wt% progesterone loading and active concentrations close to 10 mg/mL, of which approximately 80% is dissolved in the α-tocopherol. For prolonged stability, the nanoparticles are lyophilized with Pluronic F68. The nanoparticle suspensions can be reproducibly reconstituted to the original size and at higher concentrations (3X concentration) by hand agitation for 1 minute. The reconstituted progesterone dispersion can be readily expressed through a 25 gauge syringe needle. This formulation can allow for administration of large amounts of progesterone in small volumes.

This approach to formulating progesterone is also applicable to other water-insoluble steroids, of which are common therapeutics to disease areas such as inflammation, cancer, and neurological disease. Potential markets include patients in need of pharmaceutical treatment of such diseases.

A major focus on our research is on using self-assembly to construct nanoparticles for drug delivery and imaging. Our work is highly interdisciplinary as many of the projects involve joint advisors and collaborations with researchers at NIH, Argonne National Labs, CNRS in France, in addition to corporate sponsored research.

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